

In re Appln. of Kovesdi et al.  
Application No. 09/599,997

*The Advisory Action*

The Office issued an Advisory Action on January 24, 2003. A Request for Continued Examination was filed on February 21, 2003, requesting entry of the Amendment of December 27, 2002. In the Advisory Action, the Office maintained the rejection under 35 U.S.C. § 103(a) of claims 1, 2, 21, and 24-27 as allegedly being obvious in view of the combined disclosures of U.S. Patent 6,288,024 (herein referred to as "the Bouck reference") and U.S. Patent 5,827,702 (herein referred to as "the Cuthbertson reference"). The Office also maintained the rejection under 35 U.S.C. § 103(a) of claims 1-12, 15, 21, and 24-27 as allegedly being obvious in view of the Bouck reference, the Cuthbertson reference, U.S. Patent 6,113,913 (herein referred to as "the Brough '913 patent"), and U.S. Patent 6,225,113 (herein referred to as "the Brough '113 patent"). Finally, the Office maintained the rejection under 35 U.S.C. § 103(a) of claims 1, 2, 18-21, and 24-27 as allegedly being obvious in view of the Bouck reference, the Cuthbertson reference, and U.S. Patent 5,962,311 (herein referred to as "the Wickham reference"). Reconsideration of these rejections is hereby requested.

The Office has indicated in the Advisory Action that the rejection of claims 13 and 14 over the Bouck reference and the Cuthbertson reference in view of the Brough '913 patent and the Brough '113 patent is withdrawn.

*Discussion of the Advisory Action*

The Office has maintained the rejection of claims 1, 2, 21, and 24-27 under 35 U.S.C. § 103(a) as allegedly being obvious in view of the Bouck reference and the Cuthbertson reference. In response to the Amendment of December 27, 2002, the Office contends that Applicants are "essentially arguing that because the Bouck and Cuthbertson references teach various alternatives not specifically directed to the claimed invention that these teachings teach away from the claimed invention because the references must be considered as a whole." Applicants address the comments set forth in the Advisory Action below.

Applicants do not assert that the Bouck and Cuthbertson references teach away from the presently claimed invention. A consideration of the cited references *as a whole* reveals that the presently claimed invention is unobvious over the combination of the cited references inasmuch as there is no teaching or reasonable suggestion *in the cited references* to combine their disclosures in the *precise manner* required to result in the present invention. As discussed in the Amendment of December 27, 2002, the Federal Circuit has held that combining prior art references without evidence of a suggestion,

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teaching, or motivation to combine the references, even where all elements of the claimed invention are taught in the prior art, "simply takes the inventor's disclosure as a blueprint for piecing together the prior art to defeat patentability --the essence of [impermissible] hindsight." *In re Dembiczak*, 175 F.3d 994, 999, 50 U.S.P.Q.2d 1614, 1617 (Fed. Cir. 1999). The Federal Circuit emphasized that "the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing [i.e., actual evidence] of the teaching or motivation to combine prior art references." *In re Dembiczak*, 175 F.3d at 999, 50 U.S.P.Q.2d at 1617. Applicants maintain that neither the Bouck reference nor the Cuthbertson reference teaches *the desirability of combining the teachings of the two references*, let alone in the precise manner necessary to provide the present invention. The Office has provided no actual evidence of a motivation to combine the prior art references, as required by the Federal Circuit. Accordingly, the present inventive adenoviral vector must be considered as unobvious in view of the Bouck and Cuthbertson references.

However, in order to advance prosecution and not in acquiescence of the rejection, Applicants have amended claim 1 to recite the limitations of claims 4 and 6, thereby specifying that the present inventive replication defective adenoviral vector lacks all or part of the E1 region and all or part of the E4 region (see Amendment of December 27, 2002). As the Office admits that "Bouck et al. and Cuthbertson do not specifically teach particular types of replication defective adenoviral vectors" (see page 7 of Paper No.8), the combination of the Bouck reference and the Cuthbertson reference, therefore, does not render obvious the subject matter of amended claim 1. Applicants, therefore, request that the rejection of claims 1, 21, 24-27 under Section 103(a) be withdrawn.

The Office also has maintained the rejection of claims 1, 2, 18-21, and 24-27 under 35 U.S.C. § 103(a) as allegedly obvious in view of the Bouck reference, the Cuthbertson reference, and the Wickham reference. The Office contends in the Advisory Action that Applicants have not addressed the teaching of the Wickham reference relied upon in the rejection and, therefore, the arguments presented in the Amendment of December 27, 2002, are not persuasive. However, the pending claims cannot be considered as obvious in view of the Bouck or Cuthbertson references for the reasons set forth above. There is no teaching or provided motivation in either reference to combine the teachings of the references as alleged by the Office. The Wickham reference simply does not supply the requisite teaching or motivation. In particular, the Wickham reference does not teach or suggest an adenoviral vector comprising a nucleic acid sequence encoding PEDF, and there is no suggestion in the Wickham reference to

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combine what teachings are provided therein with the Bouck reference and/or the Cuthbertson reference, let alone in the precise manner necessary to provide the present invention. Put simply, the combination of the Bouck, Cuthbertson, and Wickham references does not render obvious the presently claimed invention.

The Office has maintained the rejection of claims 1-12, 15, 21, and 24-27 under 35 U.S.C. § 103(a) as allegedly obvious in view of the Bouck reference, the Cuthbertson reference, the Brough '913 patent, and the Brough '113 patent. The Office has acknowledged in the Advisory Action that the Brough '913 and '113 patents were not properly cited with respect to at least instant claims 13 and 14. However, even if the Brough '931 and '133 patents are prior art to the instant claims, it is not obvious to make or use the adenoviral vector of the pending claims in view of the Bouck reference, the Cuthbertson reference, the Brough '913 patent, and the Brough '113 patent.

In particular, the Office relies upon the Brough '913 patent for the alleged disclosure of recombinant adenoviral vectors deficient in the E1A or E1B regions in combination with a deficiency in the E2 region and/or the E3 region and/or the E4 region. The Office relies on the Brough '113 patent for the alleged disclosure of recombinant adenoviral vectors deficient in the E4 region and comprising a gene encoding a trans- or cis-acting factor. The Brough '913 and '113 patents do not teach or suggest an adenoviral vector comprising a nucleic acid sequence encoding PEDF as presently claimed. As such, the Brough '913 and '113 patents do not satisfy the aforementioned deficiencies of the Bouck and Cuthbertson references, which also do not teach or suggested the presently claimed adenoviral vector. In addition, the Brough '913 and '113 patents do not provide the motivation and direction to combine the disclosures of Bouck and Cuthbertson references, let alone in the precise manner necessary to provide the present invention.

In view of the foregoing, Applicants submit that the present inventive replication defective adenoviral vector, which comprises a nucleic acid encoding PEDF or a therapeutic fragment thereof and lacks all or part of the E1 region and all or part of the E4 region, is not obvious in view of the combination of reference cited by the Office. Applicants request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

#### *Conclusion*

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of

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the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent.

Respectfully submitted,



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Date: March 11, 2003

#### CERTIFICATE OF MAILING

I hereby certify that this RESPONSE TO ADVISORY ACTION (along with any documents referred to as being attached or enclosed) is being filed with the United States Postal Service on the date shown below via facsimile to Examiner Terry McKelvey, Group Art Unit 1636, at 703-308-4242.

Date: \_\_\_\_\_

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